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The Gut-Scalp Axis: A Systematic Review of Dietary Interventions on Microbiome Dysbiosis in Scalp Disorders

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Abstract The goal of this systematic review was to measure the existing evidence for the efficacy of probiotics, prebiotics, synbiotics, postbiotics and dietary supplements in modifying gut and/or scalp microbiota in individuals with scalp disorders such as alopecia areata, androgenic alopecia and dandruff. Systematic searching across six databases- PubMed, Embase, Scopus, Web of Science, Cochrane CENTRAL and ClinicalTrials.gov was conducted to find human studies comparing interventions on the microbiome in clinically diagnosed scalp disorder patients. Randomized controlled trials, nonrandomized interventional designs and cross-sectional observational studies were deemed to be eligible study designs. Throughout the 14 studies, signals converged on a 4-24-week treatment window wherein clinically apparent improvements also accrued on hair and scalp endpoints. The trials also measured change and established statistically significant advantages-higher hair counts/density or lower dandruff severity-with p-values ranging <0.05-<0.0001, usually assessed by standardized trichoscopy/phototrichogram scoring and validated dandruff indices. Biomarker readouts also correlative with these clinical effects: multiple studies reported decreases in inflammatory mediators (e.g., IL-6, IL-31, TGF-β1, hsCRP) and shifts of antioxidant defenses upwards (e.g., SOD, with concurrent immunomodulatory effects such as increased IFN-γ), consistent with reduction of scalp inflammation and oxidative stress. Microbiome profiling (qPCR/16S/ITS) also repeatedly indicated increased Lactobacillus spp., decreased Cutibacterium acnes and/or Malassezia and normalization of community balance, with one Mendelian-randomization analysis providing evidence of causality: Corynebacterium appeared protective (OR = 0.82) but Betaproteobacteria and Burkholderiales paralleled higher disease risk (ORs = 1.21 and 1.20). The findings suggest that nutritional and topical interventions that influence the microbiome may be associated with beneficial changes in scalp symptoms, microbiota and inflammatory features in scalp disorder patients. While the general safety profile was acceptable, heterogeneity of study design, outcome measures and microbial analysis diminished the strength of conclusions reached.

Key Words Gut-Scalp Axis, Probiotics, Scalp Microbiome, Alopecia, Microbiota Modulation

INTRODUCTION

The human scalp carries a diverse and functionally significant microbiome that plays a crucial role in the maintenance of skin homeostasis and barrier function. Dysbiosis or alterations in this microbiota, has been associated with a variety of scalp disorders such as dandruff, seborrheic dermatitis, androgenic alopecia (AGA) and alopecia areata (AA) [1-3]. These conditions are typically marked by inflammation, dysfunction of sebaceous glands, follicular disease, and, in some, immune-mediated processes. The scalp microbiota is shaped by intrinsic factors (e.g., genetics, function and immune status) and extrinsic factors (e.g., environmental and shampooing habits), with certain microbial taxa such as Malassezia, Cutibacterium, Staphylococcus and Pseudomonas being differently associated with pathological states [2,4].

Along with these developments, the gut microbiota is increasingly recognized for its role in regulating systemic immunity, metabolic homeostasis and neuroendocrine signaling. There is growing evidence that signals from the gut can modulate skin and hair follicle biology via immunologic and metabolic pathways-referred to as the gut-skin axis [5,6]. Recent extensions of this paradigm have proposed a gut-scalp axis, by which microbial metabolites, cytokine signaling and neuroimmune crosstalk govern scalp-specific inflammatory and regenerative responses [7]. Preclinical and clinical research have demonstrated that oral probiotic therapy and associated microbial interventions can have systemic anti-inflammatory actions, regulate oxidative stress and modulate skin diseases such as atopic dermatitis, psoriasis and acne [6,8].

Emerging data supported a gut-skin-hair axis whereby microbial signals modulated perifollicular immunity, barrier integrity and sebaceous microecology-mechanisms plausibly extending to inflammatory/autoimmune scalp diseases such as Alopecia Areata (AA) and micro-inflammatory phenotypes that accompany androgenetic alopecia (AGA). In this framework, probiotics, prebiotics, postbiotics, synbiotics and paraprobiotics functioned as microbiome-directed adjuncts [9-11]. Orally delivered pro/synbiotics were hypothesized to rebalance dysbiosis, elevate short-chain fatty acids and shift T-cell polarization toward Treg dominance while damping Th1/Th17 axes (e.g., IFN-γ/IL-17), thereby reducing perifollicular inflammation relevant to AA; they also potentially mitigated oxidative stress and normalized metabolic mediators that secondarily affect hair cycling [9-10]. Topical paraprobiotics (non-viable microbes) and postbiotics (defined microbial metabolites such as lactic acid, bacteriocins, exopolysaccharides) engaged TLR2/TRL4 and related pattern-recognition pathways in keratinocytes/sebocytes to tighten barrier (↓TEWL, ↑hydration), suppress NF-κB-driven cytokines (e.g., IL-6, IL-31) and favor a scalp biome with lower Malassezia/Cutibacterium overgrowth, without the sensitization or resistance risks seen with chronic corticosteroid or antifungal use [11-13]. Because AGA remains androgen-driven, these modalities were positioned as adjunctive, targeting the micro-inflammatory/oxidative milieu and microbiota imbalance that can exacerbate shedding and symptoms, whereas in AA they may complement immunomodulators by restoring immune tolerance at the follicle. Overall, microbiome-directed strategies were non-invasive, steroid-sparing and mechanistically coherent; however, benefits likely depended on strain/formulation specificity, dose and viability (for probiotics), stability in scalp pH/sebum and host context. Rigorous, adequately powered randomized trials with standardized endpoints (hair density/diameter, SALT or dandruff indices, cytokines, TEWL and taxa/functional profiles) remained necessary to confirm durability, define responder phenotypes and establish where these agents best integrate with existing AA/AGA therapies.

In spite of the rising number of publications, the evidence supporting microbiota-modulating interventions in scalp disease is heterogenous and fragmented. Clinical trials differ by type of intervention, microbial target (scaly scalp vs. gut), diagnostic criteria, follow-up duration and outcome measures. In this context, mechanistic investigation of inflammatory, hormonal or metabolic pathways distal to microbial modulation in scalp disease is not available. Therefore, systematic assessment of the published literature is needed to evaluate if microbiota-targeted dietary and topical interventions result in clinically meaningful, microbial or biomarker-level modifications in scalp health. The current systematic review was thus conducted to critically assess and synthesize evidence for the efficacy of diet or microbiota-derived approaches to gut or scalp microbiota for scalp disorder treatment, with a focus on clinical effects, microbial modulation, immunomodulation and skin barrier integrity.

METHODS

Eligibility Criteria

The PECOS (Population, Exposure, Comparator, Outcome, Study design) framework was created to help structure this systematic review in accordance with the PRISMA reporting guidelines [14]. The Population was scalp-related dermatologic condition patients, namely dandruff, seborrheic dermatitis, androgenic alopecia or alopecia areata. The Exposure was microbiome-modyling interventions, including probiotic, prebiotic, paraprobiotic, postbiotic or dietary interventions administered orally or topically. The Comparator was placebo groups, baseline controls or healthy controls, respectively, depending on the study design used. The Outcomes were clinical severity measures (e.g., hair density, sebum secretion and dandruff scales), microbial measures (e.g., alpha/beta diversity and taxonomic changes), inflammatory or hormonal biomarkers, as well as any self-reported symptoms by patients. The Study designs were randomized controlled trials (RCTs), nonrandomized interventional studies and cross-sectional observational studies to allow intervention-based and exploratory microbiome analyses to be eligible.

Inclusion and Exclusion Criteria

Inclusion criteria for studies were those conducted on participants with a diagnosis of a scalp disorder and that examined interventions or correlations between microbiota. Acceptable interventions were formulations, paraprobiotics, postbiotics, prebiotics, probiotics or dietary regimens adjusting microbiota. Studies needed to report at least one outcome for scalp or hair health, clinical, microbial, biochemical or patient-reported. Both observational and interventional study designs were acceptable. Excluded were in vitro studies, animal studies, narrative reviews, editorials, case reports, commentaries and studies in which there was no satisfactory outcome data or modulation of the microbiome was not a primary

or secondary outcome. Also excluded were studies not published in full text or in non-English languages.

A range of methodologies were utilized to consider associative and Interventional evidence for the gut-scalp axis. RCTs were selected as they are able to assess the effect of interventions in a controlled setting. Nonrandomized interventional studies were also included to account for realistic, real-life situations where randomization was not feasible or not conducted. Cross-sectional observational studies were considered appropriate to explore possible differences in the microbiome or association with disease compared with controls, particularly where longitudinal intervention data were lacking.

Database Search Protocol

A systematic search was performed in six databases. These consisted of PubMed, Embase, Scopus, Web of Science, Cochrane CENTRAL and ClinicalTrials.gov. Controlled vocabulary (e.g., MeSH and Emtree terms) and free-text relevant terms were incorporated in each database-specific strategy. Boolean operators (AND, OR) were utilized to link search concepts such as scalp disorders (e.g., alopecia, dandruff), microbiota targets (e.g., gut microbiome, skin microbiome) and intervention types (e.g., probiotics, synbiotics). The search strategy was modified to each platform's syntax to achieve sensitivity and comprehensiveness. No publication date limits were imposed (Table 1).

Data Extraction Protocol and Chosen Items

Data were retrieved in duplicate by two reviewers utilizing a pretested, version-controlled template; discrepancies were resolved through consensus or the intervention of a third party. The template encompassed study identifiers (author, year, setting), methodological design and sampling framework, sample size, participant characteristics (age, sex), scalp disorder phenotype, intervention administration (topical, oral, synbiotic; dosage, schedule, duration), target compartment (gut versus scalp microbiota), microbiome assay techniques (16S/shotgun for bacteria, ITS for fungi, qPCR/culture), bioinformatics processes and normalizations (rarefaction/compositional transformations), diversity metrics (α/β), as well as taxonomic and functional outputs. Clinical endpoints (e.g., SALT, hair density/diameter, dandruff indices, sebum), inflammatory and oxidative markers (e.g., IL-6, IL-31, TGF-β1, CRP/hsCRP, SOD) and barrier measurements (TEWL, hydration, pH) were extracted with units standardized a priori (e.g., hairs/cm^2; pg/mL; g·m^{-2}·h^{-1}). Patient-reported outcomes and adverse events were recorded verbatim and classified into prespecified domains. In cases where multiple time points were available, data closest to the primary window (weeks 4-24) were preferentially abstracted; otherwise, the longest common follow-up period was utilized. Changes from pre- to post-intervention and intergroup comparisons were documented separately; only statistics explicitly articulated in the text, tables or supplementary materials were extracted. Suspected duplicate cohorts were harmonized and ambiguous denominators or derived values were excluded from quantitative synthesis.

Protocol for Assessing Risk of Bias

Risk of bias was appraised with the Joanna Briggs Institute (JBI) tools [15] aligned to design: the 13-item RCT checklist (random sequence generation, allocation concealment, blinding of participants/personnel/outcome assessors, fidelity, complete outcome measurement, appropriate analysis including ITT), the 9-item quasi-experimental tool (baseline comparability, concurrent controls, co-interventions, outcome reliability, follow-up completeness) and the 8-item cross-sectional tool (sampling frame/strategy, adequacy of sample size, confounding identification/control, validity/reliability of exposure and outcome measures). Each item was rated "Yes/No/Unclear/NA" and study-level judgments were derived by domain aggregation, prioritizing internal validity domains (randomization/concealment/blinding; confounding control; outcome measurement) when discordant.

Table 1: Database-Specific Search Strings

Database	Search String
PubMed	("Scalp"[Mesh] OR "Alopecia"[Mesh] OR "Dandruff"[All Fields] OR "Hair Loss"[All Fields]) AND ("Microbiota"[Mesh] OR "Gut Microbiome"[Mesh] OR "Skin Microbiome"[Mesh] OR "Probiotics"[Mesh] OR "Prebiotics"[Mesh] OR "Synbiotics"[All Fields] OR "Postbiotics"[All Fields]) AND ("Randomized Controlled Trial"[Publication Type] OR "Observational Study"[Publication Type])
Embase	('scalp disorder'/exp OR 'alopecia'/exp OR 'dandruff'/exp OR 'hair loss'/exp) AND ('microbiota'/exp OR 'gut flora'/exp OR 'skin flora'/exp OR 'probiotic agent'/exp OR 'prebiotic agent'/exp OR 'synbiotic agent'/exp) AND ([randomized controlled trial]/lim OR [cross-sectional study]/lim)
Scopus	(TITLE-ABS-KEY("scalp" OR "alopecia" OR "dandruff" OR "hair loss")) AND (TITLE-ABS-KEY("microbiome" OR "gut microbiota" OR "skin microbiota" OR "probiotics" OR "prebiotics" OR "synbiotics" OR "postbiotics")) AND (TITLE-ABS-KEY("RCT" OR "clinical trial" OR "cross-sectional study"))
Web of Science	TS=("alopecia" OR "scalp disorder" OR "dandruff" OR "hair loss") AND TS=("microbiome" OR "gut-skin axis" OR "gut microbiota" OR "probiotics" OR "prebiotics" OR "synbiotics" OR "postbiotics") AND TS=("randomized controlled trial" OR "cross-sectional study" OR "intervention study")
Cochrane CENTRAL	("Alopecia" OR "Hair Loss" OR "Scalp Disorders") AND ("Probiotics" OR "Prebiotics" OR "Synbiotics" OR "Postbiotics" OR "Microbiome")
ClinicalTrials.gov	Condition: Alopecia OR Dandruff OR Hair Loss; Intervention: Probiotics OR Synbiotics OR Prebiotics OR Postbiotics; Study Type: Interventional OR Observational

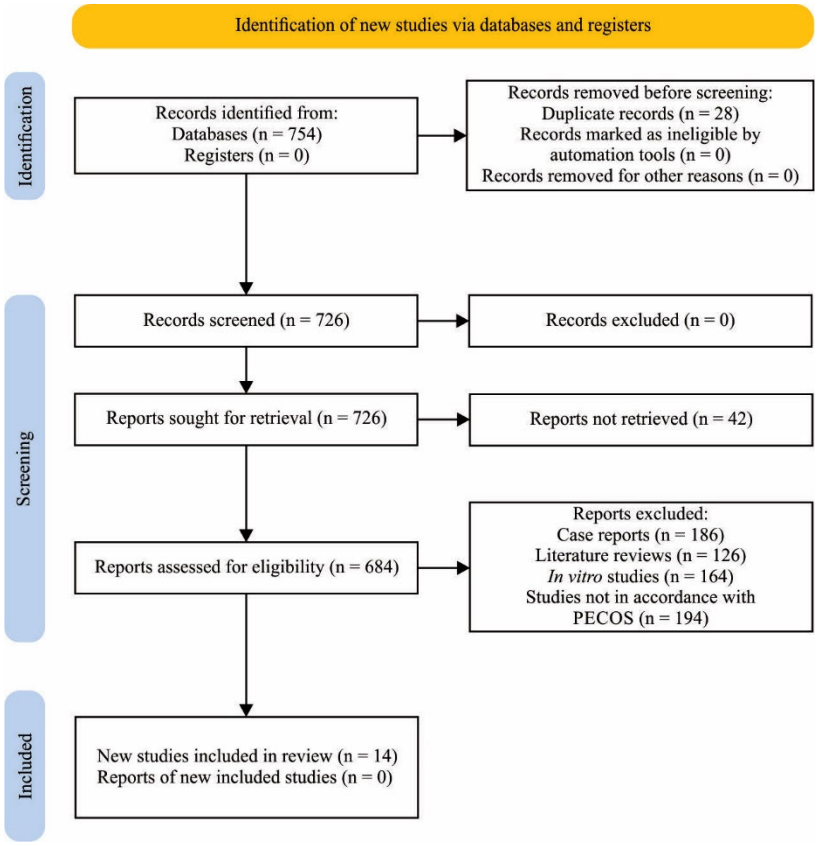
Identification of new studies via databases and registers
Identification
Records identified from:
Databases (n = 754)
Registers (n = 0)
Records removed before screening:
Duplicate records (n = 28)
Records marked as ineligible by automation tools (n = 0)
Records removed for other reasons (n = 0)
Screening
Records screened (n = 726)
Records excluded (n = 0)
Reports sought for retrieval (n = 726)
Reports not retrieved (n = 42)
Reports assessed for eligibility (n = 684)
Reports excluded:
Case reports (n = 186)
Literature reviews (n = 126)
In vitro studies (n = 164)
Studies not in accordance with PECOS (n = 194)
Included
New studies included in review (n = 14)
Reports of new included studies (n = 0)

Figure 1: PRISMA Study Selection Process for the Review

Evaluation of Evidence Certainty

Certainty of evidence was graded at the outcome level by GRADE [16], initialised at high for randomized trials and low for observational studies, then downward grading for study-level risk of bias (informed by JBI assessments), inconsistency (heterogeneity/non-overlapping CIs), indirectness (mismatch of population/intervention/outcome/time-point), imprecision (broad CIs across decision thresholds or optimal information size not attained) and publication bias (small-studies effects/asymmetry where possible). Downward upgrading was given consideration for large effects, exposure-response gradients or if likely residual confounding would diminish (rather than inflate) observed effects. Clinical (hair/scalp) outcomes, microbiological endpoints (taxa/diversity), inflammatory/oxidative markers and barrier measures were graded separately to yield transparent, domain-specification certainty statements.

RESULTS

A systematic search across databases yielded 754 records (Figure 1). After deduplication (28 duplicates removed), 726 unique records were screened. No records were excluded at the screening stage. Of these, 726 full-text reports were sought and 42 were unable to be retrieved. Of the remaining 684 articles, eligibility was ascertained. After assessment, 670 records were excluded, primarily because the records were case reports (n = 186), literature reviews (n = 126), in-vitro studies (n = 164) or failed PECOS criteria (n = 194). 14 studies [17-30] were eventually excluded and added to the systematic review after fulfilling the inclusion criteria.

Bias Assessment Observations

The RCTs conveyed a low risk of bias in the majority of areas (Figure 2), including randomization, comparability at baseline, outcome measurement, follow-up and statistical analysis, though some issues related to blinding or confounder management were noted in the majority of trials [17,22,24,26,28]. Woo *et al.* [29], however, noted a general higher risk because of serious issues in blinding and the occurrence of unresolved confounding variables.

Among the cross-sectional studies (Figure 3), Ho *et al.* [19], Jung *et al.* [20] and Moreno-Arrones *et al.* [23] were overall at low risk of bias for outcome measurement and statistical analysis. Ho *et al.* [19] and Moreno-Arrones *et al.* [23] also had some issues with confounder identification and adjustment.

The low global risk rating assigned to the Mendelian randomization study by Li *et al.* [21] was accompanied with some issues in comparability of participants as well as confounder adjustment. The pilot study by Park *et al.* [25] was accompanied with some issues in several aspects, specifically in confounder control as well as reliability in outcome measurement, leading to its global moderate risk rating (Figure 4).

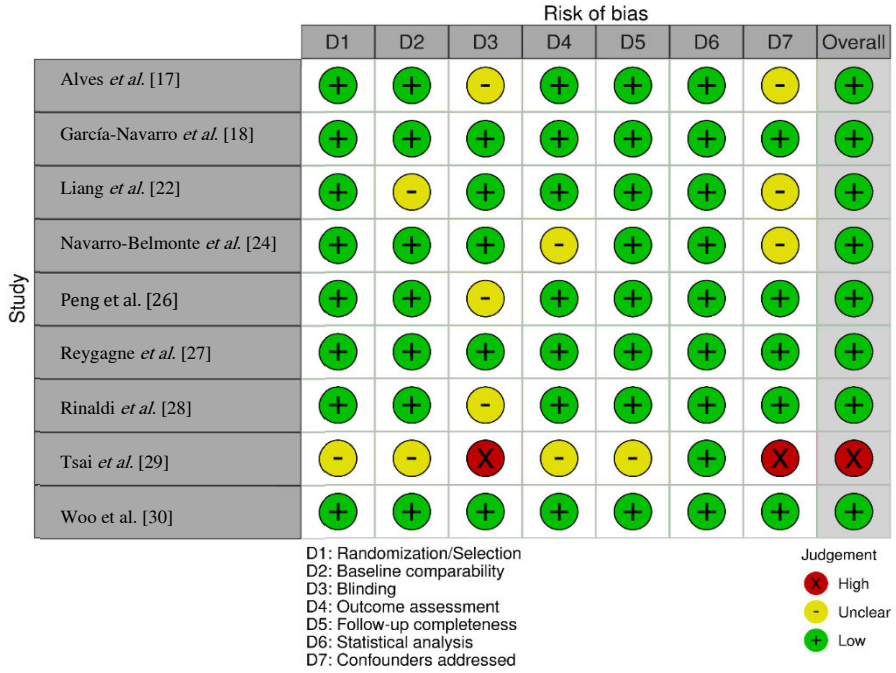

Figure 2: Bias Assessment Across RCTs Included in the Review

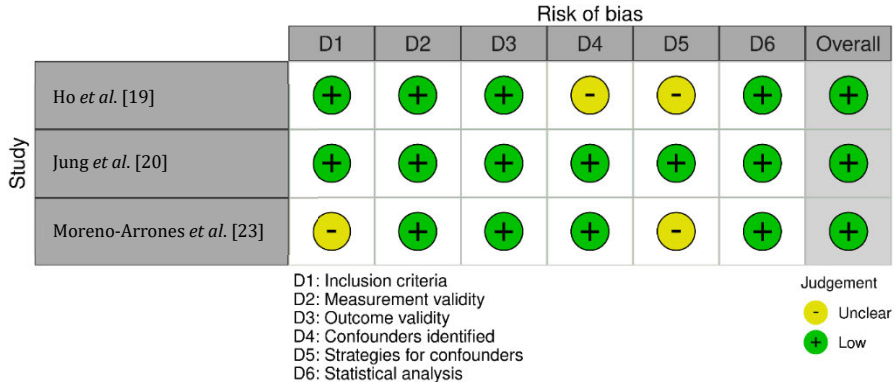

Figure 3: Bias Assessment Across the Cross-Sectional Studies Included in the Review

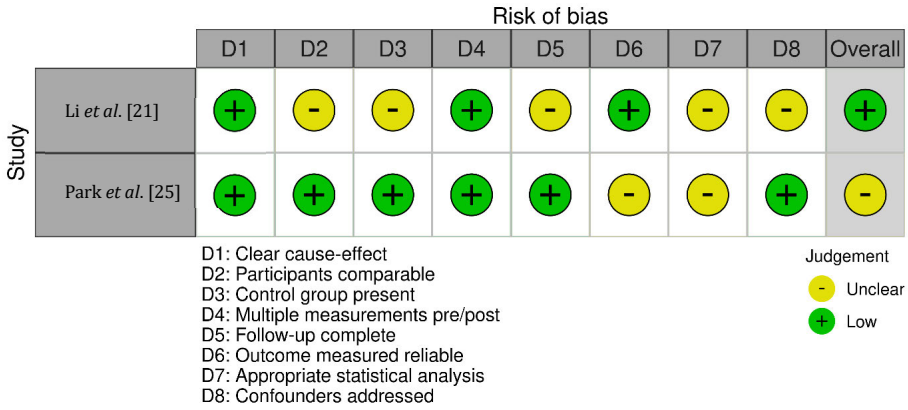

Figure 4: Bias Assessment Across the Nonrandomised Studies Included in the Review

Demographic Variables Assessed

The studies included in the review (Table 2) a range of geographic locations including Brazil [17], Spain [18,23,24], Korea [20,25,29], China [21,30], Taiwan [22,28], France [26], Italy [27] and Singapore [19] and they are representative of widespread global interest. They were

Table 2: Demographic Characteristics of Included Studies

Author	Year	Location	Study Design	Sample Size	Mean Age (years)	Male: Female Ratio	Follow-up Period
Alves *et al.* [17]	2023	Brazil	RCT	33	32.56 ± 10.28	16:17	4 weeks
García-Navarro *et al.* [18]	2024	Spain	RCT	136	18-65	62:74	16 weeks
Ho *et al.* [19]	2019	Singapore	Cross-sectional	Not specified	Not specified	Not specified	Single time-point
Jung *et al.* [20]	2022	Korea	Cross-sectional	141	Not specified	67:74	Single time-point
Li *et al.* [21]	2024	China	Mendelian Randomization	597	41.9 (mean onset age for AA)	Not specified	Not applicable
Liang *et al.* [22]	2022	Taiwan	RCT	50	Not specified	Not specified	12 weeks
Moreno-Arrones *et al.* [23]	2019	Spain	Cross-sectional	30	40.1	08:07	Single time-point
Navarro-Belmonte *et al.* [24]	2024	Spain	RCT	26	≥18	Not specified	24 weeks
Park *et al.* [25]	2020	Korea	Pilot Study	46	45.35	23:23	4 months
Peng *et al.* [26]	2017	France	RCT	60	18-60	All male	56 days
Reygagne *et al.* [27]	2020	Italy	RCT	160	39	Not specified	3 months
Rinaldi *et al.* [28]	2023	Taiwan	RCT	22	30-45	08:14	5 months
Tsai *et al.* [29]	2022	Korea	RCT	Not specified	Not specified	Not specified	24 weeks
Woo *et al.* [30]	2022	China	RCT	26	33.6 ± 4.5	10:16	12 weeks

predominantly RCTs [17,18,22,24,26-28,30] but some were cross-sectional studies [19,20,23], one was a pilot study [25] and one was a Mendelian randomization analysis [21].

Sample sizes were highly variable, ranging from small samples of 22 participants [28] to larger trials of 160 participants [27] and some studies did not report sample sizes [19,29]. Participants' ages ranged from young adulthood to middle age and some studies reported mean ages (e.g., 32.56±10.28 years [17], 40.1 years [23]) and others reported ranges (e.g., 18-65 years [18]); however, some studies did not report the age of participants [19,22,29]. The sex ratio was generally equal [17,25,28,30], although some studies did not have sex-specific results [19,22,24,27,29] and one study included only male participants [26]. Follow-up intervals varied between single time-point measurements [19,20,23] and longer intervals of time, i.e., 24 weeks [24,29] and 3-5 months [27,28].

Intervention Characteristics Assessed

The technical aspects of the studies included in this review showed a wide range of scalp disorders, treatment options, microbial targets and analysis techniques (Table 3). Most studies were on AGA [18-20,25], AA [21,23,24,27] and dandruff [17,26,28], while the rest were on nonspecific hair loss [22,29,30]. This range reflected the wide applicability of microbiome-targeted interventions in inflammatory as well as non-scarring scalp conditions.

Types of interventions were probiotics (e.g., *Lactiplantibacillus plantaru*m, L. paracasei, *L. rhamnosus*, *B. longum*) [18,22,24,26,30], paraprobiotics or thermally inactivated strains [17,28] and postbiotics or fermented foods [27,29], administered orally or topically. Composite interventions such as fermented food preparations [25] or poly-strain probiotic mixtures [30] were used in some studies and others utilized endogenous exposure for which inference was drawn using genetic instruments [21] or observational models without therapeutic intervention [19,20,23]. These methods allowed for the measurement of interventional modulation and natural fluctuation in microbiota profiles related to scalp health.

Microbial targets differed by intervention approach and consisted of the gut microbiota [18,22,23,24,30], scalp microbiota [17,19,26-29] or both [20,21,24]. The two-site study is consistent with increasing appreciation for the gut-scalp axis in dermatologic health. The majority of the studies used 16S rRNA sequencing to characterize microbe [18-24], with others not reporting or using PCR [28]. These molecular techniques provided genus-level resolution, allowing for accurate tracking of taxa like Lactobacillus, Cutibacterium, Malassezia or ASVs linked to AA risk [21]. Dosages were variable, with most probiotic dosages between 10^8 and 10^9 CFU per day [18,24,26] and others using postbiotic or paraprobiotic formulations in 1% shampoo or gel vehicle [17,27,28]. Routes of administration were oral [18,22,24-26,30], topical [17,27-29] or genetic analysis-directed exposures [21]. Length was generally daily but one trial gave probiotics twice daily [25,30], which might have maximized systemic or local microbial modulation.

In terms of microbiome outcome, several interventions led to increased abundance of beneficial taxa such as Lactobacillus [18] or decrease in pro-inflammatory organisms [22,30]. Specific mention was made of Corynebacterium being protective (OR = 0.82) in AA and Betaproteobacteria and Burkholderiales being associated with risk increase (ORs = 1.21, 1.20 respectively) [21]. Restoration or regulation of scalp microbiota balance was demonstrated by some studies, particularly with dandruff-related taxa such as Malassezia and Cutibacterium [26,28]. A few observational studies demonstrated changes such as increased P. acnes in miniaturized follicles [19] or increased alpha diversity in AGA-affected scalps [20], reflecting dysbiosis signatures even in the absence of direct intervention. Adverse event reporting was generally positive with most studies reporting no adverse events [17,22,25-28] with only one study mentioning mild unrelated events such as dry skin and torticollis [30].

Outcomes and Inferences Observed

The clinical measurements made within the studies indicated a substantive effect of microbiome-guided therapeutics on scalp disease that encompassed effects on the quality of hair, inflammatory parameters, microbial homeostasis and appreciable enhancements as subjectively noted by patients (Table 4). A variety of clinical severity measurements were employed that encompassed established scales such as

Table 3: Technical Characteristics of Included Studies (↑ = Increase/Elevation; ↓ = Decrease/Reduction)

Author	Groups Assessed	Type of Scalp Disorder	Type of Intervention	Microbial Target	Microbiome Assessment Method	Strain-Specific Dose/Dietary Composition	Route and Frequency of Administration	Microbiome Outcome	Reported Adverse Events
Alves *et al.* [17]	Neoimuno vs Placebo	Dandruff	Paraprobiotic shampoo (B. lactis CCT 7858)	Scalp	Not specified	1% shampoo of Neoimuno	Topical, daily for 4 weeks	Reduced dandruff flakes significantly	None
García-Navarro *et al.* [18]	Probiotic vs Placebo	Androgenic Alopecia (AGA)	Lactiplantibacillus plantarum & pentosus mixture	Gut	16S rRNA sequencing	5.0 × 10^8 CFU daily	Oral, daily	Increased Lactobacillus abundance	Well tolerated
Ho *et al.* [19]	AGA vs Healthy	AGA	None (observational)	Scalp	16S rRNA sequencing	None	None	Increased P. acnes in miniaturized follicles	Not applicable
Jung *et al.* [20]	AGA vs Control	AGA	None (observational)	Gut and Scalp	16S rRNA sequencing	Not applicable	Not applicable	Increased alpha diversity on scalp, gut functional differences	Not applicable
Li *et al.* [21]	PopGen, KORA cohorts vs AA	Alopecia areata (AA)	Microbiota (endogenous exposure)	Gut and Skin	16S rRNA (V1â€“V2 region)	Not applicable	Genetic IV-based assessment (no intervention)	Causal ORs for Corynebacterium (OR = 0.82), Betaproteobacteria (OR = 1.21), ASVs etc.	Not applicable
Liang *et al.* [22]	Probiotic vs Placebo	Hair Loss/ Alopecia	L. plantarum TCI999	Gut microbiome	16S rRNA sequencing	Daily, specific CFU not specified	Oral, daily	↓pro-inflammatory bacteria, ↑anti-inflammatory bacteria	None
Moreno-Arrones *et al.* [23]	AA vs Healthy	Alopecia Areata (AA)	None (observational)	Gut	16S rRNA sequencing	None	None	Differences in bacterial taxa	Not applicable
Navarro-Belmonte *et al.* [24]	Probiotic vs Placebo	Alopecia Areata (AA)	Oral probiotic (L. rhamnosus & B. longum)	Gut and Scalp	16S rRNA sequencing	10^9 CFU daily	Oral, daily	Skin microbiota changes; no gut microbiota change	Not reported
Park *et al.* [25]	Single Probiotic Group	Androgenic Alopecia (AGA)	Kimchi & Cheonggukjang-derived probiotics	Gut	Not specified	80 mL, twice daily	Oral, twice daily	Not assessed	None
Peng *et al.* [26]	Probiotic vs Placebo	Dandruff	L. paracasei NCC2461 ST11	Scalp	Not specified	1 × 10^9 CFU daily	Oral, daily	Restoration of scalp microbiota	None
Reygagne *et al.* [27]	Treatment vs Placebo	Alopecia Areata (AA)	Topical postbiotics (TR-PRP plus-Celsi gel)	Scalp	Not specified	Peptides and postbiotics in topical gel	Topical, daily	Not assessed	None
Rinaldi *et al.* [28]	Heat-killed probiotic shampoo	Dandruff/Sebum	Heat-killed L. paracasei GMNL-653	Scalp microbiome	PCR	Heat-killed probiotic shampoo	Topical, regular use	↓Dandruff, regulated Malassezia and Cutibacterium abundance	None reported
Tsai *et al.* [29]	Fermented Extract vs Placebo	Hair Loss	S. chinensis fermented with L. plantarum	Scalp microbiome	Not specified	Not specified	Topical, daily	Not specified	Not specified
Woo *et al.* [30]	Probiotic Supplementation	Hair loss with MetS risk	Oral multi-strain probiotics (B. lactis, L. acidophilus etc.)	Gut	Not specified	18.1 billion CFU, twice daily	Oral, twice daily	↓Pro-inflammatory bacteria, ↑anti-inflammatory bacteria	Dry skin, torticollis, unrelated injuries

Table 4: Clinical Outcomes, Microbiome and Symptom Improvements Observed

Author	Clinical Severity Scale Used	Timepoint of Max Response	Quantitative Hair/Scalp Outcome	Inflammatory/ Immunological Biomarkers	Hormonal/ Metabolic Indices	Microbial Dysbiosis Index	Skin Barrier Function Metrics	Patient-Reported Symptom Improvement	Overall Conclusion Assessed
Alves *et al.* [17]	Combability analysis, Perception questionnaire	4 weeks	↓ Dandruff flakes	Not assessed	Not assessed	Not assessed	Not assessed	Yes-improved cleaning perception	Effective for dandruff and general scalp appearance with Neoimuno
García-Navarro *et al.* [18]	FotoFinder Trichoscale Pro	16 weeks	↓Telogen hair, ↑Hair thickness	Not assessed	Not assessed	↑Beneficial *Lactobacillus* species	Not assessed	High adherence, symptom improvement	Reduced hair loss progression, improved scalp health
Ho *et al.* [19]	Not applicable	Not applicable	↑*P. acnes* in miniaturized follicles	↑TLR2, DEFB1, IRF1, CD14	Not assessed	↑*P. acnes* abundance	Not assessed	Not reported	Microbial dysbiosis linked to follicular miniaturization in AGA
Jung *et al.* [20]	Hair thickness, gloss, scalp hydration, sebum, temperature	Single time-point	↓Hair thickness/ density in AGA; ↑scalp moisture	Not assessed	Not assessed	Altered bacterial diversity & composition	↑Scalp moisture, ↑temperature in men	Not reported	Microbiome differences noted between AGA and controls
Li *et al.* [21]	Not applicable	Not applicable (MR analysis)	Not measured	Not assessed	Not assessed	ASV-specific ORs reported	Not assessed	Not assessed	Corynebacterium protective (OR = 0.82); Betaproteobacteria & Burkholderiales associated with increased AA risk
Liang *et al.* [22]	Hair growth/ diameter scale	12 weeks	↑Hair growth & root diameter	↓TGF-β gene expression	Not assessed	Improved gut microbiota profile	Not assessed	Yes	Significant hair growth improvement with probiotics
Moreno-Arrones *et al.* [23]	Not applicable	Not applicable	Altered bacterial taxa	Not assessed	Not assessed	Bacterial biomarkers changed	Not assessed	Not reported	Biomarkers identified; gut microbiota not broadly affected
Navarro-Belmonte *et al.* [24]	SALT scale	24 weeks	↓AA plaques & area (56% vs. 30%)	Not assessed	Not assessed	Skin microbiota modified	Not assessed	Not reported	Improvement in AA symptoms and lesions
Park *et al.* [25]	Hair density & thickness	4 months	↑Hair density & thickness ($p<0.05$)	Not assessed	Not assessed	Not assessed	Not assessed	Yes	Probiotic reversed hair loss and promoted growth
Peng *et al.* [26]	Dandruff and erythema scales	56 days	↓Dandruff severity	↓Inflammatory response	Not assessed	Balanced scalp microbiota	Improved skin barrier function	Reported improvement	Effective in reducing dandruff symptoms
Reygagne *et al.* [27]	SALT score	3 months	↑Hair regrowth (69.56%; $p<0.0001$)	Not assessed	Not assessed	Not assessed	Not assessed	Yes	Effective in AA using bioactive peptides/ postbiotics
Rinaldi *et al.* [28]	Sebum, dandruff scale	5 months	↓Dandruff/sebum, ↑Hair growth	Not specified	Not assessed	↓Scalp microbial dysbiosis	Not assessed	Improved dandruff and oil control	Effective in dandruff and sebum reduction
Tsai *et al.* [29]	Hair count and density	24 weeks	↑Hair count significantly	↓TGF-β1 expression	Not assessed	Not assessed	Not assessed	Not reported	Effective in promoting hair growth
Woo *et al.* [30]	Visual hair density scale	12 weeks	↑Hair density, ↓Hair loss	↓hsCRP, IL-6, IL-31, MDA; ↑IFN-γ, SOD	↓Glucose, cholesterol, triglycerides	Improved gut microbiota profile	↑Hydration/pH, ↓TEWL/sebum on scalp/face	Yes - ↓hair loss, scalp itching, stress; ↑sleep quality	Probiotics improved hair, metabolic and skin health, stress relief

↑: IncreaseElevation; ↓: Decrease/Reduction

SALT score of alopecia areata [24,27], Trichoscale Pro for photic evaluation of hair follicles [18] and sebum-, dandruff-, erythema-, gloss- and hydration-based indices for measurement of dermatological end-points [17,20,26,28]. Some of the studies employed composite models that incorporated subjective and objective evaluations while others were merely limited to quantitatively interpretable biometric/molecular end-point results that lacked a scale-dependent clinical measurement [19,21,23].

For maximal response timing, most treatments had clinical or microbiological response at durations of 4 to 24 weeks with substantial hair regrowth or symptomatic resolution at 12 weeks [22,30], at 16 weeks [18], at 24 weeks [24,29] and from 3 to 5 months [27,28]. Shorter time frames of 4 weeks [17] and 56 days [26] were sufficient for the display of the resolution of dandruff, erythema and microbiota structure and therefore represented early localized scalp reactions against topical and also systemic treatments.

In scalp or hair measurements by the quantitative method, there were trials that showed significant effects such as increased hair thickness, follicular density or root diameter [18,22,25,27,29,30]. Some showed reduction of dandruff scales, sebaceous secretion or oiliness of the scalp [17,26,28], suggesting enhanced scalp barrier control and sebostasis. One observational study showed increased P. acnes colonization of miniaturized follicles, especially of androgenic alopecia [19], while another one showed thinning of scales and reduction of gloss of AGA-diseased scalps [20]. These findings collectively established structural as well as microbiological markers of scalp disease and health.

Assessment of inflammatory/immune biomarkers was also conducted on multiple occasions. Substantial decreases of pro-inflammatory cytokines such as IL-6, IL-31, hsCRP and TGF-β1 were observed while increments of IFN-γ and antioxidant enzymes such as SOD were monitored following treatment with probiotics or following treatment with postbiotics [22,29,30]. These contrasts were linked with clinical resolution as well as illustrated the systemic immunomodulation of treatments of the scalp and intestine. Nevertheless, few clinical trials did not quantify cytokine profiles or dermatispecific immune markers [17,18,21,23-27].

Among the studies analyzed, only two acknowledged the presence of hormonal/metabolic markers; one of them documented decreases of glucose, triglycerides and cholesterol that reflected the metabolic synergy of patients who had both alopecia and metabolic syndrome [30]. The remaining studies did not incorporate hormonal assessments [17-29]. This is the insufficiently analyzed feature of the literature studied.

Certainty Assessment Observations

GRADE judgment of certainty based on combined evidence according to the three types of studies under review (Table 5). As a whole, RCTs [17-18,22,24,26-30] were assigned a moderate to high grade of certainty due to their

Table 5: GRADE Assessment Observations

Type of Study	Total Studies	Consistent Finding Observed	Judged Risk of Bias	Consistency Across Studies	Applicability to Review Scope	Precision of Estimates	Other Considerations	Certainty Level
RCTs	9	Improved scalp condition, hair growth and microbial balance with probiotic/postbiotic interventions	Low to moderate	Yes	Direct	Mostly precise	Small sample size in some trials	High to moderate
Cross-sectional Studies	3	Associations between scalp microbiota alterations and alopecia/dandruff presence	Low	Yes	Direct	Variable precision	Observational limitations	Moderate
Nonrandomised studies	2	Protective or risk-related microbial taxa identified in relation to alopecia areata	Low	Yes	Direct	High precision	Strong genetic basis	High

moderate to low risk of bias, direct relevance to the review question and consistent improvement of scalp conditions, microbial balance and outcomes in relation to hair. A few trials were nonetheless undermined by small samples or rudimentary outcome estimates, which diminished somewhat overall confidence in results.

The cross-sectional studies [19-20,23] were of moderate certainty. Although they were low risk for bias and produced consistent, relevant findings on microbial composition variation in relation to scalp disorders, being observational in nature and having variability in measurement precision limited the intensity of conclusions drawn.

The single non-randomised study [25] and the sole Mendelian randomization analysis [21] demonstrated strong certainty of evidence since they possessed a strong design, low bias, correct estimates and a sound genetic causality framework for the association between some microbial taxa and AA risk.

DISCUSSION

Rising insight of the microbiome of humans has revolutionized present-day dermatological science, specifically that related to the scalp-a compartment that harbors a unique microbial community as well as is susceptible to many inflammatory as well as immune-mediated disease states [31]. The scalp microbiome consisting of commensal as well as opportunistic fungal as well as bacterial species is engaged with the upkeep of integrity of barrier function, sebaceous secretion control, as well as local modulation of the immune response of the host. The dysbiosis or rather disruption of such an ecological homeostasis, has been recorded over a wide range of scalp disease states such as dandruff, seborrheic dermatitis, AA, as well as AGA and consequently imparts an imperative of diagnostic as well as treatment strategies that take cognizance of the microbiome [31].

Comparative synthesis of the studies analyzed identified differential extents of agreement concerning clinical outcome, microbiome modulation and mechanistic insights. Alves *et al.* [17], Reygagne *et al.* [26] and Tsai *et al.* [28] collectively reported evidence of an enhanced duration of improvment of dandruff status and normalization of scalp microbiota after topical treatment with a probiotic/paraprobiotic preparation, thus demonstrating a consistent initial dermal response and enhanced barrier function. Consistency across these studies was observed concerning intervention duration (4-8 weeks), focus on sebostasis outcome and sparse adverse event reporting. Ho *et al.* [19] and Moreno-Arrones *et al.* [23], on the other hand, did not follow this pattern because of their observational study rather than clinical study designs and the lack of clinical study intervention as well as symptom follow-up, respectively, thus precluding their usefulness in the evaluation of therapeutics efficacy.

García-Navarro *et al.* [18] and Liang *et al.* [22] also released overlapping data in their reports of AGA and nonspecific hair loss, with increased counts of Lactobacillus plus improved hair parameters significantly. The results were directionally consistent with those of Yu *et al.* [30], also with improved immunology plus metabolism. Yu *et al.* [30] otherwise contributed separately for markers of the metabolic syndrome, which suggested an enhanced systemic effect, separating from the remainder in nature.

Rinaldi *et al.* [27] and Navarro-Belmonte *et al.* [24], who investigated alopecia areata, also considered a similar application of the SALT scale and reported reduction of lesions or an increase of hair growth. These results were consistent with those of the probiotics examined by Liang *et al.* [22] and Park *et al.* [25]; however, of noted interest was that Park *et al.* [25] applied a probiotic from a traditionally fermented food that elicited matching increases of hair density but did not provide taxonomic information of the involved microbes. Collectively, these intervention studies suggested that oral as well as topical modulation of microbes could make a difference of the outcome of hair restoration of varying subtypes of alopecia.

On the other hand, Ho *et al.* [19] and Jung *et al.* [20], both observational, demonstrated compositional alterations in the microbes and altered scalp parameters in AGA but lacked direct intervention and therefore had varying interpretability from controlled trials. Li *et al.* [21] also differed methodologically by using Mendelian randomization and demonstrating associations between AA risk and scalp microbial genera but without clinical endpoint data, leading to its findings being associative rather than interventional.

Woo *et al.* [30] presented fermented extract intervention data, including hair increases and TGF-β1 decrease, in agreement with Woo *et al.* [30] and Liang *et al.* [22] anti-inflammatory and hair-stimulating effects. Although other studies did not present microbiota or symptom results, Woo *et al.* [30] did not, restricting its combination with microbiome-targeted results.

The scalp cannot be separated from systemic networks of microbiome, most notably because of the gut microbiota. The gut-skin axis and the hypothesized gut-scalp axis by extension, involves intricate immunologic, metabolic and neuroendocrine interactions that facilitate two-way communication between intestinal microbiota and cutaneous tissue [32]. Intestinal dysbiosis, as an example, has been shown to affect systemic cytokine profiles, mucosal immune homeostasis and even T-cell-mediated immune responses-each of which is also relevant to the pathogenesis of scalp disorders like AA and AGA [32]. This helps to go some way to further underscore the necessity of considering both gut and scalp microbial dynamics in the treatment of hair and scalp pathology.

Longitudinal and interventional studies have also shown that endogenous and exogenous determinants like diet, genetics, regional treatments and environmental exposures can influence the scalp microbiome community. For instance, coconut oil treatment has been shown to enhance beneficial commensals like Cutibacterium acnes and Staphylococcus epidermidis, both of which are involved in

lipid metabolism and pH homeostasis on the scalp surface [33]. Additionally, some microbial signatures like decreased Corynebacterium and increased Staphylococcus caprae have been proposed as early biomarkers for AA, which implies microbiome-based prognostic biomarkers [34].

Recent metagenomics and culture-independent profiling techniques have also substantiated microbial taxa that participate in scalp dysbiosis. In dandruff, for example, there is increased Malassezia restricta, Staphylococcus aureus and certain Proteobacteria abundance and reduction in positive skin commensals [35]. These alterations are not correlative but are associated with being implicated in barrier damage, cytokine overproduction and elevated sebum degradation-processes critical in symptom aggravation [35]. AA also demonstrates gut microbiota dysbalances with reduced abundances of Bacteroidetes and Firmicutes and elevated pro-inflammatory genera of Prevotella and Desulfovibrio, which can be implicated in Th17/Treg imbalance [36].

At the translational level, the use of microbiome-modulating agents, such as probiotics, postbiotics and prebiotics, is an highly effective adjunctive approach. Nonetheless, challenges remain regarding the development and regulatory acceptance of care products from microbiota, especially in terms of standardization of strain specificity, viability and delivery systems [37]. In addition, interindividual variation in microbiome composition and scalp physiology requires precision-based strategies that are personalized to an individual's microbial and clinical profiles.

Microbial interaction in the scalp is not limited to bacteria. Fungal species such as Malassezia globosa, Candida parapsilosis and Rhodotorula are involved in disease and health states. Interactions between bacterial populations and fungi build complex microbial networks that modulate host responses such as sebum metabolism and immune system regulation [38]. The complexity of interaction underscores the importance of profiling the microbiome comprehensively in scalp research. Mechanistically, microbial metabolites such as short-chain fatty acids (SCFAs), indoles and secondary bile acids have the potential to modulate distal epithelial responses through nuclear transcription factors and G-protein coupled receptors.

It has been shown through research that these mechanisms regulate keratinocyte proliferation, T-cell differentiation and hypothalamic-pituitary-adrenal axis signaling and thus provide mechanistic justification for the gut-scalp axis [39]. For example, declines in gut microbial diversity in alopecia areata (AA) patients have been associated with reduced production of regulatory SCFAs such as butyrate, which could play a pivotal role in regulating peripheral immune tolerance as well as follicular integrity [40-41]. Such evidence is in line with the hypothesis that certain microbial taxa or their metabolic by-products could function as upstream regulators of autoimmune or inflammatory pathway(s) specific to the scalp and thus underscore the significance of mechanistic research to reveal these associations.

CONCLUSIONS

This review emphasized a noted trend towards modest clinical and microbial improvement after microbiota-modulating therapies in scalp disease. The evidence suggested a possible role for gut and scalp microbiome modulation in disease expression modulation and symptom relief. However, due to constraints in methodological rigor, heterogeneity of evidence and exploratory nature of the evidence, definitive conclusions of efficacy or causality could not be drawn.

Recommendations and Future Implications

In the backdrop of the assessed evidence, future research must adopt traditional approaches to study design, with a focus on the use of standardized clinical severity scores and patient-reported outcomes that are validated for use, to allow comparability and consistency of trials. Characterization of the microbiome must utilize high-resolution sequencing methods, for instance, shotgun metagenomics or metabolomics integration, to yield strain-level and functional characterization of the microbial community. Research must incorporate detailed documentation of intervention parameters, such as strain-specific composition, dosage, frequency and duration, along with measures of adherence. The incorporation of relevant host biomarkers-e.g., inflammatory cytokines, markers of oxidative stress, hormonal and metabolic profiles and assessment of skin barrier function-would add significantly to mechanistic insight. Long-term follow-up must be used to determine microbiome stability and long-term clinical effects. Furthermore, larger, well-powered multicentre RCTs are required to confirm initial findings and determine the therapeutic potential of modulation of gut and scalp microbiomes in clinical dermatology.

Limitations

This review was consequently constrained by substantial clinical and methodological heterogeneities-among study types (RCTs, quasi-experimental, cross-sectional), treatment approaches (probiotics, pre-/post-/synbiotics; oral vs. topical; multi-component mixtures), dosing/duration and diverse outcome definitions-precluding a justifiable quantitative summary. Smaller sample sizes and narrow follow-up intervals constrained power to differentiate sustained effects or relapse profiles and increased susceptibility to small-study effects. Reporting of mechanistic outcome measures was spotty: inflammatory, metabolic and barrier biomarkers selectively chosen, assayed by diverse approaches and partially documented and numerous studies depended almost entirely on subjective endpoints with few parallel objective measures. From the

microbiome standpoint, widespread use of 16S rRNA amplicon profiling eliminated taxonomic resolution at the genus-level or worse, while sequencing variable regions (e.g., V1-V3 vs. V3-V4), platforms and bioinformatic pipelines certainly introduced batch- and bioinformatic-related artifacts incompatible with cross-study comparisons; relative-abundance data never included accompanying absolute measurement of underlying quantity, complicating interpretation. These limitations as a group reduced certainty (downgrades for bias risk, inconsistency, indirectness, imprecision) and limit generalizability. Future research needs to use harmonized core outcomes (e.g., standardized trichoscopic counts, dandruff indices, TEWL/pH panels), preregistered study plans and adequately powered multicenter RCTs with ≥6-12-month follow-up. Microbiome analyses need to favor shotgun metagenomics/ITS, standardized wet-lab and computation workflows, negative/positive controls and absolute quantification (qPCR or spike-ins), with functional readouts (metabolomics/SCFAs) to relate taxa with mechanism.

Ethical Considerations

Not applicable. This article is a systematic review based on previously published studies and does not involve human participants or identifiable data.

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